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10

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/339, 103	06/24/99	KILGER	C P1614-8090

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ARENT, FOX, KINTNER, PLOTKIN & KAHN PLLC
SUITE 600
1050 CONNECTICUT AVE. N.W.
WASHINGTON DC 20036-5339

EXAMINER

HORLICK, K

ART UNIT	PAPER NUMBER
1656	13

DATE MAILED: 03/21/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)
	09/339,103	KILGER ET AL.
	Examiner Kenneth R Horlick	Art Unit 1656

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 11 January 2001.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-144 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-144 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. 08/991,184.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) Notice of References Cited (PTO-892) 18) Interview Summary (PTO-413) Paper No(s). _____ .
- 16) Notice of Draftsperson's Patent Drawing Review (PTO-948) 19) Notice of Informal Patent Application (PTO-152)
- 17) Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____. 20) Other: _____

Art Unit: 1656

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-126, 134-137, 143, and 144 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 34-58 of copending Application No. 09/357,166 in view of Gelfand et al. (US 5,310,652) and Birch et al. (5,677,152). This is a provisional obviousness-type double patenting rejection.

The copending claims are drawn to methods and kits for simultaneously amplifying and sequencing nucleic acids, requiring two different polymerases, wherein one has a higher affinity towards a chain-terminating nucleotide relative to the other.

The copending claims do not encompass direct application of the methods/kits to RNA wherein at least one of the polymerases has reverse transcriptase activity, nor modification of said methods/kits to include a polymerase-inhibiting agent.

Gelfand et al. disclose a one-tube, one-polymerase amplification of target RNA sequences using a polymerase with reverse transcriptase activity (see, for example, the abstract).

Birch et al. disclose the advantageous use of a polymerase-inhibiting agent, including antibodies and various anhydrides, in nucleic acid amplifications (see, for example, the abstract and Fig. 1).

One of ordinary skill in the art would have been motivated to modify the methods of the copending claims by application towards RNA using a polymerase with reverse transcriptase activity, and/or application of a polymerase-inhibiting agent, because Gelfand et al. disclosed the advantages of combined reverse-transcription and

Art Unit: 1656

amplification, and Birch et al. disclosed the benefits of using such an agent in amplification reactions. In other words, these would have been logical, straightforward applications to achieve expected improvements. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to make the claimed kits and carry out the claimed methods.

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-126, 134-137, 143, and 144 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koster et al. (US 5,928,906) in view of Gelfand et al. (US 5,310,652) and Birch et al. (5,677,152).

These claims are drawn to methods and kits for simultaneously amplifying and sequencing nucleic acids, requiring two different polymerases, wherein one has a higher affinity towards a chain-terminating nucleotide relative to the other, further comprising: direct application to RNA wherein at least one of the polymerases has reverse transcriptase activity; and/or use of a polymerase-inhibiting agent.

Koster et al. disclose methods and kits for simultaneously amplifying and sequencing nucleic acids, requiring two different polymerases, wherein one has a higher affinity towards a chain-terminating nucleotide relative to the other (see especially column 3, lines 25-57, column 7, lines 43-67 and column 8, lines 1-6, and Example 1 in columns 11-12).

This patent does not disclose DNA polymerase-mediated reverse transcription coupled to PCR amplification, nor the use of polymerase-inhibiting agents.

Gelfand et al. disclose a one-tube, one-polymerase amplification of target RNA sequences using a DNA polymerase with reverse transcriptase activity (see, for example, the abstract).

Birch et al. disclose the advantageous use of a polymerase-inhibiting agent, including antibodies and various anhydrides, in nucleic acid amplifications (see, for example, the abstract and Fig. 1).

One of ordinary skill in the art would have been motivated to modify the method

of Koster et al. by application towards RNA using a polymerase with reverse transcriptase activity, and/or application of a polymerase-inhibiting agent, because

Gelfand et al. disclosed the advantages of combined reverse-transcription and amplification, and Birch et al. disclosed the benefits of using such an agent in amplification reactions. In other words, these would have been logical, straightforward applications to achieve expected improvements. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to make the claimed kits and carry out the claimed methods.

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY THE AMENDMENT

3. Claims 129, 130, 133, and 142 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 129 and 130 are confusing because of the language “are reduced at different time,” at the end of claim 129.

B) Claims 133 and 142 are confusing because of improper Markush language (“or” rather than “and”).

4. Claims 132, 133, 141, and 142 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koster et al. (US 5,928,906) in view of Gelfand et al. (US 5,310,652) and Birch et al. (5,677,152), and further in view of Hill (US 5,525,492).

The further limitations of these claims involve agents that lower the melting point of DNA, which is not taught in the previously-discussed references.

Hill discloses the use of a polar aprotic solvent such as DMSO in nucleic acid amplification reactions to facilitate amplification of G-C rich sequences (see column 2, lines 5-40).

One of ordinary skill in the art would have been motivated to use a melting point-lowering agent such as DMSO in the methods and kits as rejected previously because Hill taught that this advantageously provided for amplification of sequences of high G-C content. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to make the claimed kits and carry out the claimed methods.

5. Claims 127-131 and 138-140 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7 and 8 of copending Application No. 09/577,047. Both sets of claims overlap in subject matter, particularly with respect to inhibition of both polymerases with agents and release of the polymerases from inhibition at different times.

6. With respect to the above rejections, the arguments of the response filed 01/11/01 have been fully considered, but are not found persuasive. While the response points to a declaration filed in parent application 08/991,184 as support for Koster being a non-enabling reference, said declaration was previously found to be insufficient to establish non-enablement. The response also argues there would not have been reasonable expectation of success for combining the "technically challenging" simultaneous amplification/sequencing method of Koster and the polymerase-inhibition methodology of Birch et al.; however, no specific argument is provided as to why the skilled artisan might have suspected the polymerase-inhibition means of Birch et al. would interfere with Koster's method. The claims require only one polymerase inhibiting

agent, and it is submitted that the skilled artisan would have reasonably expected use of such an agent to work in Koster's method in the manner indicated by Birch et al.

7. Claims 127-131 and 138-140 are free of the prior art, but are rejected for other reasons. These claims require two different polymerase-inhibiting agents which can inhibit different thermostable DNA polymerases, which is not taught or suggested in the prior art. No claims are allowable.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Art Unit: 1656

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kenneth R Horlick whose telephone number is 703-308-3905. The examiner can normally be reached on Monday-Thursday 6:30AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Margaret Parr can be reached on 703-308-2454. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Kenneth R. Horlick, Ph.D.
Kenneth R Horlick
Art Unit 1656

March 14, 2001

KENNETH R. HORLICK
PRIMARY EXAMINER
GROUP 1656/600